

Substitute Specification - Marked-Up Copy

CoQ₁₀-CONTAINING PRELIPOSOMES AND PREPARATION THEREOFcontaining preliposomes and preparation thereofField of the Of The Invention

The present invention relates to the fields field of Pharmaceutics pharmaceuticals and ~~cosmetic~~, cosmetics. More specially, the present invention relates to CoQ₁₀-containing preliposomes, and more particularly, in particular, relates to the preparation method and the application of CoQ₁₀-containing preliposomes which ~~contains~~ contain spongiamine.

BACKGROUND of the Of The Invention

CoQ₁₀ (conenzymeQ₁₀, ubiquinone) is a kind of a liposoluble quinone compound, which has the same character as a ~~with~~ vitamin. The ~~prominence~~ prominent function of CoQ₁₀ is anti-oxidation and ~~to clean the~~ cleaning free radicals, radicals. CoQ₁₀ is one of the most important functional components used in many anti-aging products at present. It ~~is~~ has been proved experimentally ~~by the~~ experiment that CoQ₁₀ can accelerate the metabolism of ~~the~~ skin, accelerate the transport of cellular respiration chain and ~~the~~ ATP production of facial and hand skin. ~~the skin of face and hand. Simultaneity,~~ Simultaneously, CoQ₁₀ can inhibit ~~the~~ peroxide oxidation of the skin lipid, and consequently nourish and activate the skin. It is reported that ~~the~~ body slimming ~~lotion~~ lotions and UV expert ~~cream~~ creams which

contains contain CoQ₁₀ ~~has~~ have obvious ~~effect~~ effects on preventing the formation of furrows, whitening the complexion, ~~increasing~~ increasing the elasticity of the skin and so on. CoQ₁₀ not only ~~protect~~ protects the skin, but also ~~prevent and cure the~~ prevents and cures skin diseases of the human ~~beings~~ being. It is ~~proved by the~~ experiment has been experimentally proven that CoQ₁₀ has obvious therapeutic ~~effect~~ effects on photoallergy, dermatitis, hair-lose, ~~bedsore, ulcer and wound of~~ bedsores, ulcers, wounds of the skin, hyperpigmentation and so on. As ~~Because~~ the molecular structure of CoQ₁₀ has an unsaturated double bond, CoQ₁₀ is extremely unstable and is easy to ~~be oxidated~~ oxidize and becomes decomposed by the oxygen and light in the ~~air,~~ and air. In addition, heating or contacting CoQ₁₀ with metal ~~ion~~ ions will accelerate its decomposition. ~~it to be decomposed~~. As a result, the content of CoQ₁₀ in the ~~product has~~ products becomes decreased, ~~or~~ and the activity of CoQ₁₀ ~~lost quickly,~~ then affect is quickly lost, adversely affecting the quality and actual effect of the ~~products~~ product. In addition, CoQ₁₀ is a liposoluble compound, which makes it difficult to mix will result in difficulty in mixing with the ~~water-solubility~~ water-soluble cosmetics. ~~cosmetic~~. The foregoing disadvantages of CoQ₁₀ extremely restrict the development and application of CoQ₁₀.

Liposomes are ~~Liposome~~ is composed by of hydrophilic ~~bursa~~ bubble bubbles which ~~consists with~~ consist of lecithoid double molecular ~~layers~~ layer. Liposomes have characteristics that ~~Liposome has the character to~~ improve the stability of drug encapsulation, facilitate the percutaneous absorption of drugs, ~~the drug~~, prolong the time of drug action, control the drug targeting at the local pathological ~~changes part~~

parts of the body, and decrease the side effects of drugs. ~~effect of the drug~~. Thus, as drug carriers, liposomes have ~~drug carrier, liposome has~~ been widely used in pharmaceutics and cosmetics. ~~Pharmaceutics and cosmetic~~. CoQ₁₀ liposomes could improve the stability of drugs, ~~the drug~~, facilitate the percutaneous absorption of drugs, ~~the drug~~, and increase the water-solubility of drugs. ~~the drug~~. But generally being a kind of liposome ~~liposomes~~ suspension solution, CoQ₁₀ has obvious shortcomings in the stability. The reasons are as following:

1. As colloidal particulates, liposomes are ~~colloid particulate, liposome is~~ a kind of unstable thermodynamic system ~~thermodynamics instability system~~, which is easy to congregate, fuse and sedimentate, and the oxidation decompose of the lecithoid ~~causes lecithoid~~, leakage of the encapsulation drug in ~~into~~ the water, aqueous solution, etc., ~~will result~~ resulting in the instability of the liposome.

2. The instability of the structure of CoQ₁₀ ~~will make the drug~~ makes drugs more instable in the water.

3. The ratio of CoQ₁₀, liposome suspension and ~~the drug content~~ is generally fixed; however, the required content of CoQ₁₀ differs in different cosmetics. Thus, it is not convenient to mix CoQ₁₀ liposome ~~suspension~~ suspensions with ~~cosmetic~~ cosmetics which contain ~~contains~~ CoQ₁₀.

So it is necessary to find a kind of liposome ~~prescription~~ preparation which is convenient, flexible, easy to mix with ~~cosmetic~~ cosmetics which contain ~~contains~~ CoQ₁₀, in order ~~able~~ to make the ~~liposome and drug~~ liposomes and drugs more stable, and ~~able to be stored~~ storable for a long periods of time.

Disclosure of the Invention ~~The description of the invention~~

~~The~~ An object of present invention is to overcome the shortcomings of CoQ₁₀ and common CoQ₁₀ liposome, and to supply a kind of CoQ₁₀-containing preliposomes which contain ~~contains~~ spongiamine. The present invention ~~could~~ will increase the stability of CoQ₁₀ and liposomes ~~liposome~~ and make the mixing of cosmetics ~~mixing~~ more flexible and convenient.

The CoQ₁₀-containing preliposomes made according to the ~~by~~ present invention are a kind of solid preparation which are the granular and ~~lyophilized, before~~ lyophilized. Before using, water is added to the CoQ₁₀-containing ~~preliposomes, after~~ preliposomes. After hydration and surging, ~~the~~ CoQ₁₀-containing preliposomes ~~could~~ can become CoQ₁₀-containing liposomes.

The structure of the CoQ₁₀-containing preliposomes ~~mentioned in~~ of the present invention contain ~~contains~~ spongiamine ~~with the~~ at a concentration at 0.1% ~ 20% (W/W). Spongiamine can further facilitate the percutaneous absorption and improve the effect of CoQ₁₀ in cosmetics. ~~the cosmetic.~~

The CoQ₁₀-containing preliposomes which contain spongiamine ~~mentioned in~~ according to the present invention are prepared by the following methods and processes. ~~method and process:~~

1) CoQ₁₀, spongiamine and other lipid ~~component~~ components are melted by heating or are dissolved by proper organic solvent(s) so that a ~~solvent, and~~ lipid solution is made,

2) ~~Use A~~ A fluidized bed can be used to spray bed, make the above-mentioned lipid solution ~~sprayed on the~~ an underlay which is suspended in the middle of the fluidized ~~bed, let the~~ bed. The organic solvent is volatilized, and CoQ₁₀-containing preliposomes which contain spongiamine is obtained, ~~are got,~~

3) Make the lipid solution mentioned in step 1) and water solution which contains an underlay by known methods such as a membrane disperse dispersion method or a melt method or an infuse method, ~~and method to obtain~~ CoQ₁₀-containing liposomes which contain the underlay, ~~contains underlay are got,~~

4) Make the CoQ₁₀-containing liposomes which contain an ~~contains~~ underlay by freeze drying or spray drying, or wiping wipe off the moisture to obtain moisture, CoQ₁₀-containing preliposomes which contains spongiamine. ~~spongiamine are got.~~

The CoQ₁₀-containing preliposomes ~~mentioned in of the~~ present invention ~~contains~~ contain CoQ₁₀ ~~with the~~ at a concentration ~~at of~~ 0.2 ~ 40% (W/W). ~~After~~ (W/W), ~~after~~ restoring by adding water, the concentration of the CoQ₁₀ is at 0.1 ~ 20% (W/W).

Suitable organic solvents that can be used according to the ~~The proper organic solvents mentioned in~~ present invention include dichloromethane, trichloromethane, ether and ethanol.

The concentration of underlay used according to the ~~mentioned in~~ present invention involved in the CoQ₁₀ preliposomes which contain ~~contains~~ spongiamine is 1~80%.

Underlays that can be used according to the ~~The underlay mentioned in~~ present

invention is are selected from one of the following materials: mannitol, glucose, sorbitol, sucrose, lactose, fucose, sodium chloride and polyvinylpyrrolidone.

The lipid components that can be used according to the component mentioned in present invention include spongiamine and at least one of the following components: cholesterol, soy lecithin, yolk lecithin, hydrogenated lecithin, DSPC, DPPP, poloxamer, DMPC and non-ionic surfactant like Brij.

The materials used in according to the present invention are all commercially available. ~~bought from the market.~~

The CoQ₁₀-containing preliposomes which contain ~~contains~~ spongiamine according to the mentioned in present invention not only have the same merit as the common liposomes, ~~for example, liposomes in that they~~ increase the stability of the ~~drug, drugs,~~ facilitate the percutaneous absorption of ~~the drug, drugs,~~ and prolong the time of drug ~~action, but also~~ action. In addition, the CoQ₁₀-containing preliposomes which contain spongiamine according to the present invention have the following merits:

1. The increased ~~Increase the~~ stability of CoQ₁₀-containing liposomes allow for longer storage times. ~~liposomes, can be stored for a long time.~~

Because the ~~above mentioned~~ the preliposomes are solid ~~drug, it can~~ drugs, they overcome the shortcomings that the common liposomes have, such as congregating, sedimentating, fusing, leaking ~~congregate, sedimentate, fuse,~~ and ~~leakage and~~ so on.

2. ~~Increase the~~ The stability of the CoQ₁₀ is increased. ~~CoQ₁₀.~~

Because the ~~above-mentioned~~ the preliposomes are solid ~~drug, it could~~ drugs, the present invention can be used to make the unstable drug drugs more stable in the solid state than in the liquid state.

3. ~~Facilitate the~~ The percutaneous absorption of the CoQ₁₀ is increased.
~~CoQ₁₀.~~

~~Because the~~ The structure of the ~~above-mentioned~~ liposomes ~~contain~~ containing spongiamine according to the present invention ~~spongiamine, it could~~ obviously facilitate the percutaneous absorption of drugs. the drug.

4. ~~Can~~ The CoQ₁₀-containing liposomes of the present invention can be mixed with other components at ~~random; make it~~ at random making them easier and more convenient to formulate into cosmetics. ~~confect the cosmetic which contains~~
~~CoQ₁₀.~~

Generally, for ~~the cosmetic~~ cosmetics which ~~contains liposome, contain~~ liposomes there is a certain range of the liposome volume. If the contains of liposomes exceed the range, ~~the character~~ characteristics of the cosmetics ~~cosmetic~~ will be affected, such as viscosity, flow property, viscosity, the content of the active component and so ~~on, furthermore, on.~~ Furthermore, certain cosmetics require different amounts of the CoQ₁₀. it is different for the required content of CoQ₁₀ for ~~certain cosmetic.~~ Before use, water can be added to the CoQ₁₀-containing preliposomes which contain ~~contains~~ spongiamine according to the mentioned in present invention on demand, so as to provide liposomes which have different drug contents ~~content of drug can be got~~ to meet different cosmetic prescriptions.

prescription.

Examples

Example 1:

~~Get~~ In this example, 120g of CoQ₁₀, 50g of spongiamine, 50g of yolk lecithin, 100g of cholesterol, 100g of sucrose, were combined with enough ~~add~~ PBS (pH 7.4) to the produce a volume of 1000 ml.

~~Put~~ The CoQ₁₀, spongiamine, yolk lecithin and cholesterol from the above prescription were put into a triangle flask, ~~heat~~ heated to cause fusion, ~~store~~ and stored in a water bath at 80°C for further use. 800 ml of PBS (pH 7.4) was used to dissolve the ~~above-mentioned~~ 140g of sucrose, ~~filter, heat the filter solution~~ sucrose. The dissolved solution was filtered and heated in a water bath to reach the same temperature with the ~~liposomes solution, mix the water~~ liposome solution. The sucrose solution was mixed with the liposome liposomes solution by surging and cooled. Enough surging, then cool, add PBS (pH 7.4) was added to get produce 1000 ml of the mixed solution, after solution. A high pressure homogeneous management (50 MPa of high pressure, 10 MPa of low ~~pressure~~); pressure) was used to obtain a liposome liposomes suspension solution, ~~is got, after~~ After spray drying, a ~~kind of~~ well fluid CoQ₁₀-containing preliposomes which contained ~~contains~~ spongiamine was obtained, ~~is got~~.

Example 2:

Get In this example, 30g of CoQ₁₀, 50g of spongiamine, 30g of soy lecithin, 100g of cholesterol, 40g of poloxamer F₆₈, 200g of glucose, and 200 ml of chloral, ~~add~~ were combined with enough PBS (pH 7.4) to ~~the~~ produce a volume of 1000 ml.

~~Put~~ The CoQ₁₀, spongiamine, soy lecithin, poloxamer F₆₈ and cholesterol from the above prescription were put into a 1000 ml ~~of rockered flask, use~~ rocked flask and the chloral was used to dissolve the lipid ~~components, rotary~~ components. The resulting mixture was subject to membrane evaporate evaporation in a water bath at 25~40°C to make the lipid form a membrane layer ~~of membrane~~ at the bottom of the rocked flask. ~~Rockered flask for further use.~~ Use 800 ml of PBS (pH 7.4) was used to dissolve the ~~above mentioned~~ 200g of glucose. The solution was filtered and added to the flask containing the lipid membrane for hydration thereof using surging. ~~glucose, filter, put the filter into the above mentioned flask, hydrating and surging, add~~ Enough PBS (pH 7.4) was added to produce ~~to get~~ 1000 ml of mixed solution, ~~after solution which was subject to ultrasonic treatment (output 4, duty cycle 50%, time 10 mins), liposomes~~ mins) to produce a liposome suspension solution, is got, after After freeze drying (temperature at -50°C the degree of vacuum is 50 millitorr), a kind of loose CoQ₁₀-containing preliposomes which contain ~~contains~~ spongiamine was obtained. ~~is got.~~

Example 3:

Get In this example, 50g of CoQ₁₀, 50g of spongiamine, 60g of hydrogenated lecithin, 40g of cholesterol, 50g of poloxamer F₆₈, and 80g of fucose, 200ml of ether,

~~add~~ were combined with enough PBS (pH 7.4) to produce a volume of 1000 ml.

~~Put~~ The CoQ₁₀, spongiamine, hydrogenated lecithin, poloxamer F₆₈ and cholesterol from the above prescription were put into a 500ml of triangle flask, use flask and the ether was added to dissolve the lipid components for further use. Use 800 ml of PBS (pH 7.4) was used to dissolve the above-mentioned 80g of fucose, filter, fucose. The fucose solution was filtered and put the filter into a the triangle flask, store flask which was stored in a water bath at 30~60°C, mixing and mixed round by magnetic force at the speed of 200~1000 rpm, evaporate the organic solvent, rpm. After the organic solvent was evaporation a liposome liposomes suspension solution was obtained and freeze dried is got, after freeze drying (temperature at -50°C, the degree of vacuum is 50 millitorr), millitorr) to produce a kind of loose CoQ₁₀-containing preliposomes which contains contain spongiamine, is got.

Example 4: test of stability

~~Put~~ Samples of the three batch batches of containing spongiamine CoQ₁₀-containing preliposomes which contain spongiamine and a common CoQ₁₀-containing liposomes (the liposomes suspension before drying) were stored separately into the condition which is at a temperature of 40°C and at a relative humidity level of 75%. degree of humidity. After 0, 1, 2 and 3 months, use High Performance Liquid Chromatography (HPLC) was used to test the content of CoQ₁₀ in the preliposomes and the common liposomes, use the liposomes. The content of 0 month CoQ₁₀ in the preliposomes and the common liposomes was used as 100%, 100%

to compare the content of drug at other ~~time~~ times with the above mentioned content of CoQ₁₀, and calculate ~~get~~ the percent content of drug as the time goes by.

Table 1 lists the stability comparing ~~result~~ results of the content of CoQ₁₀ in the preliposomes and the common liposomes.

Table 1

The change percent of the content of CoQ ₁₀ (%)				
Time (mo)	0	1	2	3
Common liposomes	100.00	93.32	88.03	83.50
Preliposomes	100.00	99.86	99.53	98.76

The ~~result shows~~ results show that the content of the drug contained in the common liposomes decreased along with the time ~~obviously, however,~~ while the content of the drug contained in the preliposomes ~~didn't decreased~~ did not decrease along with the time ~~significantly, it indicated~~ significantly. This ~~indicates~~ that the CoQ₁₀-containing preliposomes which ~~contains~~ contain spongiamine could evidently improve the stability of drugs. ~~the drug.~~